

## WHAT IS CLAIMED IS:

1 ~~Sub~~ 1. A non-toxic *Pseudomonas* exotoxin A-like ("PE-like") chimeric  
2 immunogen comprising: (1) a cell recognition domain of between 10 and 1500 amino  
3 acids that binds to a cell surface receptor; (2) a translocation domain comprising an  
4 amino acid sequence substantially identical to a sequence of PE domain II sufficient to  
5 effect translocation to a cell cytosol; (3) a non-native epitope domain comprising an  
6 amino acid sequence of between 5 and 1500 amino acids that encodes a non-native  
7 epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum ("ER")  
8 retention domain that comprises an ER retention sequence.

1 2. The immunogen of claim 1 having the amino acid sequence of PE  
2  $\Delta$ E553 except that the sequence of domain Ib of PE  $\Delta$ E553 comprises the non-native  
3 epitope between two cysteine residues of domain Ib.

1 3. The immunogen of claim 1 wherein the cell recognition domain is  
2 domain Ia of PE.

1 4. The immunogen of claim 1 wherein cell recognition domain binds  
2 to  $\alpha$ 2-macroglobulin receptor (" $\alpha$ 2-MR"), epidermal growth factor ("EGF") receptor; the  
3 IL-2 receptor; the IL-6 receptor; HIV-infected cells; a chemokine receptor; a leukocyte  
4 cell surface receptor; a ligand for the IgA receptor; or an antibody or antibody fragment  
5 directed to a receptor.

1 5. The immunogen of claim 1 wherein cell recognition domain  
2 comprises amino acid sequences of a growth factor or an antibody.

1 6. The immunogen of claim 1 wherein cell recognition domain is  
2 comprised within the ER retention domain.

1 ~~Sub~~ 7. The immunogen of claim 1 wherein the translocation domain  
2 comprises amino acids 280 to 364 of domain II of PE.

1 8. The immunogen of claim 1 wherein the translocation domain is  
2 domain II of PE.

1 9. The immunogen of claim 1 wherein the ~~non-native epitope~~ domain  
2 comprises a cysteine-cysteine loop that comprises the non-native epitope.

1 10. The immunogen of claim 1 wherein the non-native epitope domain  
2 comprises an amino acid sequence encoding a non-native epitope inserted between two  
3 cysteine residues of domain Ib of PE.

1 11. The immunogen of claim 1 wherein the non-native epitope domain  
2 comprises an amino acid sequence selected from CTRPNYNKRK RIHIGPGRAF  
3 YTTKNIIGTI RQAHC (SEQ ID NO:3) or CTRPSNNTRT SITIGPGQVF YRTGDIIGDI  
4 RKAYC (SEQ ID NO:4).

1 12. The immunogen of claim 1 wherein the ER retention domain is  
2 domain III of PE comprising the mutation  $\Delta$ E553.

1 13. The immunogen of claim 1 wherein the ER retention sequence  
2 comprises REDLK (SEQ ID NO:11), REDL (SEQ ID NO:12) or KDEL (SEQ ID  
3 NO:13).

1 14. The immunogen of claim 1 which is ntPE-V3MN14 or ntPE-  
2 V3MN26.

1 15. The immunogen of claim 1 wherein the non-native epitope is an  
2 epitope from a viral, bacterial or parasitic protozoan pathogen.

1 16. The immunogen of claim 9 wherein the non-native epitope is an  
2 epitope of a V3 loop of gp120 of HIV-1.

1 17. The immunogen of claim 9 wherein the non-native epitope is an  
2 epitope of a principal neutralizing loop of a retrovirus.

1 18. The immunogen of claim 9 wherein the non-native epitope is an  
2 epitope of a major neutralizing loop of HIV-2 or a V3 loop of gp120 of HIV-1 of at least  
3 8 amino acids including a V3 loop apex.

1 19. A recombinant polynucleotide comprising a nucleotide sequence  
2 encoding a non-toxic *Pseudomonas* exotoxin A-like ("PE-like") chimeric immunogen, the  
3 PE-like chimeric immunogen comprising: (1) a cell recognition domain of between 10  
4 and 1500 amino acids that binds to a cell surface receptor; (2) a translocation domain  
5 comprising an amino acid sequence substantially identical to a sequence of PE domain II  
6 sufficient to effect translocation to a cell cytosol; (3) a non-native epitope domain  
7 comprising an amino acid sequence of between 5 and 1500 amino acids that encodes a  
8 non-native epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum  
9 ("ER") retention domain that comprises an ER retention sequence.

1 20. The recombinant polynucleotide of claim 19 which is an expression  
2 vector further comprising an expression control sequence operatively linked to the  
3 nucleotide sequence.

1 21. The recombinant polynucleotide of claim 19 having the amino acid  
2 sequence of PE wherein domain Ib of PE further comprises the non-native epitope  
3 between two cysteine residues of domain Ib.

1 22. A recombinant non-toxic *Pseudomonas* exotoxin A-like ("PE-like")  
2 chimeric immunogen cloning platform comprising a nucleotide sequence encoding: (1) a  
3 cell recognition domain of between 10 and 1500 amino acids that binds to a cell surface  
4 receptor; (2) a translocation domain comprising an amino acid sequence substantially  
5 identical to a sequence of PE domain II sufficient to effect translocation to a cell cytosol;  
6 (3) an amino acid sequence encoding an endoplasmic reticulum ("ER") retention domain  
7 that comprises an ER retention sequence and (4) a splicing site between the sequence  
8 encoding the translocation domain and the sequence encoding the ER retention domain.

1                   23.     The recombinant cloning platform of claim 22 which is an  
2     expression vector further comprising an expression control sequence operatively linked to  
3     the nucleotide sequence.

1                   24.     A method of producing antibodies against a non-native epitope,  
2     wherein the non-native epitope naturally exists within a cysteine-cysteine loop comprising  
3     the step of inoculating an animal with a non-toxic *Pseudomonas* exotoxin A-like ("PE-  
4     like") chimeric immunogen, the PE-like chimeric immunogen comprising: (1) a cell  
5     recognition domain of between 10 and 1500 amino acids that binds to a cell surface  
6     receptor; (2) a translocation domain comprising an amino acid sequence substantially  
7     identical to a sequence of PE domain II sufficient to effect translocation to a cell cytosol;  
8     (3) a non-native epitope domain comprising a cysteine-cysteine loop that contains within  
9     the loop an amino acid sequence of between 5 and 1500 amino acids that encodes a non-  
10    native epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum  
11    ("ER") retention domain that comprises an ER retention sequence.

1                   25.     The method of claim 24 wherein the cysteine-cysteine loop  
2     comprises no more than about 30 amino acids.

1                   26.     The method of claim 24 wherein the non-native epitope is an  
2     epitope of the V3 domain of HIV-1.

1                   27.     A vaccine comprising at least one non-toxic *Pseudomonas* exotoxin  
2     A-like ("PE-like") chimeric immunogen, the PE-like chimeric immunogen comprising:  
3     (1) a cell recognition domain of between 10 and 1500 amino acids that binds to a cell  
4     surface receptor; (2) a translocation domain comprising an amino acid sequence  
5     substantially identical to a sequence of PE domain II sufficient to effect translocation to a  
6     cell cytosol; (3) a non-native epitope domain comprising an amino acid sequence of  
7     between 5 and 1500 amino acids that encodes a non-native epitope; and (4) an amino  
8     acid sequence encoding an endoplasmic reticulum ("ER") retention domain that  
9     comprises an ER retention sequence.

1                   28.    The vaccine of claim 27 comprising a plurality of PE-like chimeric  
2 immunogens, each immunogen having a different non-native epitope.

1                   29.    The vaccine of claim 27 further comprising a pharmaceutically  
2 acceptable carrier.

1                   30.    The vaccine of claim 27 in the form of an immunization dose  
2 wherein the immunogen is present in an amount effective to elicit in a human subject an  
3 immune response against the non-native epitope.

1                   31.    The vaccine of claim 28 wherein the different non-native epitopes  
2 are epitopes of different strains of the same pathogen.

1                   32.    The vaccine of claim 31 wherein the non-native epitope is an  
2 epitope of the V3 loop of HIV-1 and the different strains of the same pathogen are HIV-1  
3 MN and HIV-1 Thai-E.

1                   33.    A method of eliciting an immune response against a non-native  
2 epitope in a subject, the method comprising the step of administering to the subject a  
3 vaccine comprising at least one non-toxic *Pseudomonas* exotoxin A-like ("PE-like")  
4 chimeric immunogen, the PE-like chimeric immunogen comprising: (1) a cell recognition  
5 domain of between 10 and 1500 amino acids that binds to a cell surface receptor; (2) a  
6 translocation domain comprising an amino acid sequence substantially identical to a  
7 sequence of PE domain II sufficient to effect translocation to a cell cytosol; (3) a non-  
8 native epitope domain comprising an amino acid sequence of between 5 and 1500 amino  
9 acids that encodes a non-native epitope; and (4) an amino acid sequence encoding an  
10 endoplasmic reticulum ("ER") retention domain that comprises an ER retention sequence.

1                   34.    The method of claim 33 wherein the non-native epitope comprises a  
2 binding motif for an MHC Class II molecule of the subject and the immune response  
3 elicited is an MHC Class-II dependent cell-mediated immune response.

1 35. The method of claim 33 wherein the non-native epitope comprises a  
2 binding motif for an MHC Class I molecule of the subject and the immune response  
3 elicited is an MHC Class-I dependent cell-mediated immune response.

1 36. The method of claim 33 wherein the non-native epitope is an  
2 epitope of the V3 domain of HIV-1.

1 37. The method of claim 33 wherein the vaccine is administered as a  
2 prophylactic treatment against a disease mediated by an agent bearing the non-native  
3 epitope.

1 38. The method of claim 33 wherein the vaccine is administered as a  
2 therapeutic treatment against a disease mediated by an agent bearing the non-native  
3 epitope.

1 39. A polynucleotide vaccine comprising at least one recombinant  
2 polynucleotide comprising a nucleotide sequence encoding a non-toxic *Pseudomonas*  
3 exotoxin A-like ("PE-like") chimeric immunogen, the PE-like chimeric immunogen  
4 comprising: (1) a cell recognition domain of between 10 and 1500 amino acids that binds  
5 to a cell surface receptor; (2) a translocation domain comprising an amino acid sequence  
6 substantially identical to a sequence of PE domain II sufficient to effect translocation to a  
7 cell cytosol; (3) a non-native epitope domain comprising an amino acid sequence of  
8 between 5 and 1500 amino acids that encodes a non-native epitope; and (4) an amino  
9 acid sequence encoding an endoplasmic reticulum ("ER") retention domain that  
10 comprises an ER retention sequence.

1 40. A method of eliciting an immune response against a non-native  
2 epitope in a subject, the method comprising the step of administering to the subject a  
3 polynucleotide vaccine comprising at least one recombinant polynucleotide comprising a  
4 nucleotide sequence encoding a non-toxic *Pseudomonas* exotoxin A-like ("PE-like")  
5 chimeric immunogen, the PE-like chimeric immunogen comprising: (1) a cell recognition  
6 domain of between 10 and 1500 amino acids that binds to a cell surface receptor; (2) a  
7 translocation domain comprising an amino acid sequence substantially identical to a

8 sequence of PE domain II sufficient to effect translocation to a cell cytosol; (3) a non-  
9 native epitope domain comprising an amino acid sequence of between 5 and 1500 amino  
10 acids that encodes a non-native epitope; and (4) an amino acid sequence encoding an  
11 endoplasmic reticulum ("ER") retention domain that comprises an ER retention sequence.

1 41. The method of claim 40 wherein the recombinant polynucleotide is  
2 an expression vector comprising an expression control sequence operatively linked to the  
3 nucleotide sequence.

1 42. The method of claim 40 wherein the nucleotide sequence further  
2 encodes a mammalian secretory sequence attached to the amino terminus of the  
3 immunogen.

1 43. A method of eliciting an immune response against a non-native  
2 epitope in a subject, the method comprising the steps of transfecting cells with a  
3 recombinant polynucleotide comprising a nucleotide sequence encoding a non-toxic  
4 *Pseudomonas* exotoxin A-like ("PE-like") chimeric immunogen, the PE-like chimeric  
5 immunogen comprising: (1) a cell recognition domain of between 10 and 1500 amino  
6 acids that binds to a cell surface receptor; (2) a translocation domain comprising an  
7 amino acid sequence substantially identical to a sequence of PE domain II sufficient to  
8 effect translocation to a cell cytosol; (3) a non-native epitope domain comprising an  
9 amino acid sequence of between 5 and 1500 amino acids that encodes a non-native  
10 epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum ("ER")  
11 retention domain that comprises an ER retention sequence, and administering the cells to  
12 the subject.

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